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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,032	10/05/2001	Monica Montano	27708/04003	2885

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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,032	MONTANO ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 11-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/26/02, 01/05/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Exhibit A (seq. alignment, 2 pages).

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 5-10 in the reply filed on 06/14/2004 is acknowledged.

Claims 1-4, 11-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/14/2004.

Claims 1-22 are pending. Claims 5-10 are examined on merits.

Claim Objections

Claim 10 is objected to because of the following informalities: Claim 10 recites a non-existing claim i.e. claim 25. Appropriate correction is required.

For the purpose of this Office action, the Office will treat claim 10 to depend on claim 9 instead of claim 25. However, this treatment does not relieve applicant the burden of responding to this objection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9, and 10 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 9, and 10 as written, do not sufficiently distinguish over nucleic acids, as they exist naturally because the claims do not particularly point out any non-naturally

occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "under stringent conditions " in claim 5 is a relative term which renders the claim indefinite. The term " under stringent conditions " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This written description rejection is made because the claims are interpreted as drawn to genus of nucleic acid molecules.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, the only factor present in the claims 5-7 is a partial structure i.e. "at least 200 nucleotides" of SEQ ID NO:1, or a recitation of percent identity. There is not even identification of any function associated with the partial structure. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The present claims 5-7 encompass full-length genes and cDNAs (such as differently spliced isoforms of said full-length gene) that are not further described.

There is substantial variability among the species of DNA s encompassed within the scope of the claims. They are structurally unrelated. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequences, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Since the breath of the claims as reading on genes yet to be discovered, the lack of correlation between the structure and the function of the genes, it is concluded that the written description requirement is not satisfied.

Further, claim 7 recites "The isolated polynucleotide of claim 5, wherein the nucleic acid comprises part of an expression vector, a viral genome, or liposome." The specification teaches that instant SEQ ID NO:1 is a human cDNA. The specification does not teach a fragment of SEQ ID NO:1 is a part of viral genome. In other words, the specification does not describe how an isolated polynucleotide of the base claim comprising part of an expression vector, a viral genome, or a liposome looks like. Should claiming an expression vector or a viral vector comprising the isolated polynucleotide of the base claim, or composition comprising said viral or expression vector and liposome is desired, then the claim should be drafted accordingly.

Claim 9 recites "an ERCoA3 transcript". The specification at page 5, especially the paragraph bridging pages 5 and 6 implicitly describes that "an ERCoA3 transcript" is more than the transcript encoding SEQ ID NO:2 protein. Therefore, "an ERCoA3 transcript" is interpreted as a genus of transcripts. The specification describe only one

species i.e. SEQ ID NO:1. The dependent claim 10 also drawn to "an ERCoA3 transcript is rejected for the same reason set forth in rejecting claim 9.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acid molecules, given that the specification has only described SEQ ID NO: 1, which encodes SEQ ID NO:2. Therefore, only isolated nucleic acid comprising SEQ ID NO: 1, which encodes SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims 5-7, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, and nucleic acid encoding SEQ ID NO:2 protein, does not reasonably provide enablement for any other nucleic acid molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

This scope of enablement rejection is made because the nature of the invention is interpreted as drawn to nucleic acid molecules encoding various proteins for claims 5-7, and primer set for amplifying an ERCoA3 transcript for claims 9, and 10.

The specification teaches that the new discovery disclosed in the instant application is a new human cDNA i.e. SEQ ID NO:1 nucleic acid encoding SEQ ID NO:2 protein. SEQ ID NO:2 interacts with an estrogen receptor (ER) and increases the ER-dependent transcription as shown in Fig. 5. The specification does not teach how to use the claimed nucleic acid that encodes a protein that is at least 85% to SEQ ID NO:2, wherein said protein does not have the disclosed activity. The specification does not teach the specific structures responsible for ER interaction or ER-dependent co-activation of transcription, nor provide guidance as to what changes in the structure can be made retaining co-activating activity.

It is well known in the art that even slight modifications in a peptide or protein structure can have significant and unpredictable effects on biological activity. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a

message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out biological activity and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid (including conservative substitutions) in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or even with conservative glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein.

As for claims 9, and 10, the specification at the paragraph bridging pages 5, and 6 discloses "while not identical to SEQ ID NO:2 or parts thereof, are closely identical"; this implicitly teaches that "ERCoA3" is more than SEQ ID NO:2. However, the specification does not teach what other ERCoA3 transcript(s) could amplified by the primer set from SEQ ID NO:1 and its complement. The specification provides insufficient guidance, and provides no working examples other than the transcript encoding SEQ ID NO:2. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to make the alleged discovery, not how to screen it for themselves.

Considering the unpredictable state of art, limited guidance on how to use and make the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank accession number AA687318 (24 December 1997).

The claims are interpreted as drawn to an isolated nucleic acid molecule comprising at least 200 contiguous nucleotides of SEQ ID NO:1 (claim 5), an expression vector comprising said nucleic acid molecule (claim 7), an isolated

polynucleotide comprising a complementary sequence to a portion or all of the nucleic acid sequence set forth in SEQ ID NO:1 (claim 8), and primer set comprising two primers with at least 10 nucleotides in length, wherein a first primer comprises at least two contiguous nucleotides of SEQ ID NO:1, wherein a second primer comprises at least two contiguous nucleotides of the complementary of SEQ ID NO:1, wherein the second primer is downstream of the first primer (claims 9, and 10).

GenBank accession number AA687318 teaches an isolated nucleic acid that matches 100 % to nucleotide # 741 to # 965 (total 224 nucleotides) of instant SEQ ID NO:1. Thus, GenBank accession number AA687318 meets the limitation of instant claim 5. Note the attached sequence alignment (Exhibit A).

Instant claim 7 recites "an expression vector". The specification does not define what is being encompassed by "an expression vector". Therefore, the Office turns to a couple of the textbooks to see what is encompassed by an expression vector in DNA recombinant technology art. Voet et al., (1991, Biochemistry, pages 837-839 only) teach that a DNA segment could be inserted into a vector, and the chimeric vector in a suitable host organism such as E. coli or yeast results in the production of large amounts of the inserted DNA segment. Likewise, Strachan et al., (1999, Human Molecular Genetics, Chapter 10.4 only, downloaded from url..ncbi.nlm.nih.gov on 8/13/04, total pages 6) teach at page 3 of 6, 2nd paragraph in the section 10.4.2 under the heading "Exon trapping identifies expressed sequences by using an artificial RNA splicing assay" that "an expression vector" encompasses a vector designed to express RNA from DNA. GenBank accession number AA687318 teaches an isolated nucleic

acid matching 100 % to nucleotide # 741 to # 965 of instant SEQ ID NO:1 is in a vector i.e. "pT7T3D-Pac (Pharmacia) with a modified polylinker" (note bottom 1/3 of page 1 of 2 of the GenBank accession number AA687318). It appears that the vector (i.e. pT7T3D-Pac) used to insert the isolated nucleic acid that matches 100 % to nucleotide # 741 to # 965 (total 224 nucleotides) of instant SEQ ID NO:1 appears to have T3 and/or T7 promoter capable of expressing RNA from the inserted cDNA sequence by T7 and/or T3 polymerases. Therefore it is concluded that GenBank accession number AA687318 in pT7T3D-Pac vector meets the limitation of claim 7.

As for claim 8, the intended use "for inhibiting translation of an RNA which encodes SEQ ID NO:2" is merely suggestive of an intended use and is not given patentable weight for purposes of comparing the claim with the prior art. The claim reads on an isolated polynucleotide comprising complementary to a portion or all of the nucleic acid sequence set forth in SEQ ID NO:1 *per se*. Since GenBank accession number AA687318 teaches that the isolated sequence is double stranded, a complementary sequence is also included. GenBank accession number AA687318 teaches a nucleic acid sequence comprising complementary to a portion of the nucleic acid sequence set forth in SEQ ID NO:1.

As for claims 9, and 10, the scope of claims 9, and 10 as currently construed is broadly drawn to a primer set that could hybridize to many other cDNAs unrelated to instant SEQ ID NO:1, because the claims do not define how many contiguous nucleotides of SEQ ID NO:1 should be in the claimed primers, nor do the claims define how far apart the two primers should lie in SEQ ID NO:1. Any primer that contains two

contiguous nucleotides of SEQ ID NO:1 or its complement meets the structural limitation of the claimed primers. As for the limitation "said second contiguous sequence is downstream of said first contiguous sequence", even a single nucleotide apart from each other could be "downstream". GenBank accession number AA687318 teaches at least two primers, i.e. (1) a Not I-oligo (dT) primer, and (2) "–40m13 fwd. (forward) ET from Amersham". Amersham Pharmacia Biotech 1999 catalog page 341 teaches that "–40 M13 forward primer" (at least 10 nucleotides in length) comprises a sequence, which is identical to a first contiguous sequence "TTCCCA", (i.e. nucleotide #68 to #74 of the instant SEQ ID NO:1). The "$(T)_{18}$ " in the Not I-oligo (dT) primer disclosed in GenBank accession number AA687318 (note line 3 from bottom at page 1 of 2) is a complementary to the second contiguous sequence (see the poly A tail of instant SEQ ID NO:1), wherein said second contiguous sequence is downstream of said first contiguous sequence. Thus, GenBank accession number AA687318 teaches the instantly claimed primer set. The intended use "for amplifying an ERCoA3 transcript" is merely suggestive of an intended use and is not given patentable weight for purposes of comparing the claims with the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Misook Yu

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

Exhibit A

```
            McCray Lab
            University of Iowa
            2024 University of Iowa Med Labs, Iowa City, IA 52242, USA
            Tel: 319 356 4866
            Fax: 319 356 7171
            Email: paul-mccray@uiowa.edu
            Tissue Procurement: Dr. M. J. Welsh, University of Iowa
             cDNA Library preparation: Dr. M. Bento Soares, University of Iowa
             cDNA Library Arrayed by: Dr. M. Bento Soares, University of Iowa
             DNA Sequencing by: Dr. M. Bento Soares, University of Iowa
             Clone Distribution: Researchers may obtain clones from Research
            Genetics (www.resgen.com) or from Open Biosystems
            (www.openbiosystems.com).
            Seq primer: M13 FORWARD
            POLYA=Yes.
FEATURES             Location/Qualifiers
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                     UI-CF-FN0 is a subtracted cDNA library derived from two
                     normalized Human lung epithelial cell libraries (EN1 and
                     DU1) The library was subtracted according to according to
                     Bonaldo, Lennon and Soares, Genome Research, 6:791-806,
                     1996. For additional information, contact:
                     bento-soares@uiowa.edu
                     TAG_TISSUE=Human Lung Epithelial Cell Lines untreated LPS
                     6hr to LPS 24h
                     TAG_LIB=UI-CF-FN0
                     TAG_SEQ=CTGGTCAGGT"
ORIGIN

  Query Match           27.2%;  Score 269;  DB 14;  Length 633;
  Best Local Similarity   99.3%;  Pred. No. 0;
  Matches  609;  Conservative    0;  Mismatches    2;  Indels    2;  Gaps    2;

Qy        341 GCCTCCCGGTGGCCCCGCAGCGCCTCCCGGTGGCCCTGGAGTGCAGGTCTTACCGTCCGA 400
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        401 GATCGTCCGCAACTGGGCGAGCTGTGCATGGGGCGTGGCTAAGGCCGTGGTTTGGTTACG 460
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        461 ATTGGCCAGCGGGACTTAAGTGTTGTCTCTGAAGAGCATGGACATTAGTCTGGAGGGTCC 520
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Qy        521 TGGAAGAGTGATCCCCGCCCCACCATCAAATGGCGCTTAGGTCTAGGAAGCGGGTGTGGG 580
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Qy        581 TGGGGCCTTAGGGCGAGGCGCAGACATACCCCGAAGTGGTTGGATTGTATACCGCAAGGG 640
              |||||||||||||||||||||||||||| ||||||||||||||||||||||||||||||
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Qy        641 GCTGGATCGAACCCCCCAAAGACACTGGAAGGCTGTGTGGCTGAGGAGGGCCCGGCA-AT 699
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||
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Qy        700 CCAGTGTGTCGTGGGCTTTACAGGAAAGAGCTCCACCTTC-TTGGAGTGTGCAGATGCGA 758
              |||||||||||||||||||||||||||||||||||| |||||||||||||||||||||
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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        819 TGATTTGGACCTGGGGCCTCTGGACTTCCCTGATTCTCTGCTTGCATCTCCAGCAAAGTC 878
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Qy        879 CTGTCCCGTTGGCTGCCTTCATCCACTCTCTCACTTCTCTGCCTTCAGAGTAAAATTGCA 938
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Db         93 CTGTCCCGTTGGCTGCCTTCATCCACTCTCTCACTTCTCTGCCTTCAGAGTAAAATTGCA 34

Qy        939 AGATCTGTGGTGC 951
              |||||||||||||
Db         33 AGATCTGTGGTGC 21


RESULT 11
AA687318/c
LOCUS       AA687318                395 bp    mRNA    linear   EST 24-DEC-1997
DEFINITION  nv61e01.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:1234296 3',
            mRNA sequence.
ACCESSION   AA687318
VERSION     AA687318.1  GI:2675509
KEYWORDS    EST.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 395)
  AUTHORS   NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap.
  TITLE     National Cancer Institute, Cancer Genome Anatomy Project (CGAP),
            Tumor Gene Index
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Email: cgapbs-r@mail.nih.gov
            unknown library type
            Insert Length: 966   Std Error: 0.00
            Seq primer: -40m13 fwd. ET from Amersham
            High quality sequence stop: 361.
FEATURES             Location/Qualifiers
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                     /mol_type="mRNA"
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                     /clone="IMAGE:1234296"
                     /tissue_type="germinal center B cell"
                     /lab_host="DH10B"
                     /clone_lib="NCI_CGAP_GCB1"
                     /note="Vector: pT7T3D-Pac (Pharmacia) with a modified
                     polylinker; Site_1: Not I; Site_2: Eco RI; 1st strand cDNA
                     was prepared from human tonsillar cells enriched for
                     germinal center B cells by flow sorting (CD20+, IgD-),
                     provided by Dr. Louis M. Staudt (NCI), Dr. David Allman
                     (NCI) and Dr. Gerald Marti (CBER).  cDNA synthesis was
                     primed with a Not I - oligo(dT) primer
                     [5'-TGTTACCAATCTGAAGTGGGAGCGGCCGCCTCATTTTTTTTTTTTTTTTT-3'
                     ]. Double-stranded cDNA was ligated to Eco RI adaptors
                     (Pharmacia), digested with Not I and cloned into the Not I
                     and Eco RI sites of the modified pT7T3 vector. Library
                     went through one round of normalization, and was
                     constructed by Bento Soares and M. Fatima Bonaldo."
ORIGIN

  Query Match           22.7%;  Score 225;  DB 9;  Length 395;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches  225;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        741 TGGAGTGTGCAGATGCGATCTAGGTGTGTCCACCCGATGGGAGCTGCGGGCCGGGCAGAT 800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        225 TGGAGTGTGCAGATGCGATCTAGGTGTGTCCACCCGATGGGAGCTGCGGGCCGGGCAGAT 166

Qy        801 GCTGCCCCAGTACAAAGCTGATTTGGACCTGGGGCCTCTGGACTTCCCTGATTCTCTGCT 860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        165 GCTGCCCCAGTACAAAGCTGATTTGGACCTGGGGCCTCTGGACTTCCCTGATTCTCTGCT 106
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Qy        861 TGCATCTCCAGCAAAGTCCTGTCCCGTTGGCTGCCTTCATCCACTCTCTCACTTCTCTGC 920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        105 TGCATCTCCAGCAAAGTCCTGTCCCGTTGGCTGCCTTCATCCACTCTCTCACTTCTCTGC 46

Qy        921 CTTCAGAGTAAAATTGCAAGATCTGTGGTGCAAAAAAAAAAAAAA 965
              ||||||||||||||||||||||||||||||||||||||||||||||
Db         45 CTTCAGAGTAAAATTGCAAGATCTGTGGTGCAAAAAAAAAAAAAA 1
```

RESULT 12
BM672504/c
LOCUS BM672504 300 bp mRNA linear EST 27-FEB-2002
DEFINITION UI-E-CQ1-ada-e-09-0-UI.s1 UI-E-CQ1 Homo sapiens cDNA clone UI-E-CQ1-ada-e-09-0-UI 3', mRNA sequence.
ACCESSION BM672504
VERSION BM672504.1 GI:18982402
KEYWORDS EST.
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 300)
AUTHORS Bonaldo,M.F., Lennon,G. and Soares,M.B.
TITLE Normalization and subtraction: two approaches to facilitate gene discovery
JOURNAL Genome Res. 6 (9), 791-806 (1996)
MEDLINE 97044477
PUBMED 8889548
COMMENT Contact: Soares, MB
Coordinated Laboratory for Computational Genomics
University of Iowa
375 Newton Road , 4156 MEBRF, Iowa City, IA 52242, USA
Tel: 319 335 8250
Fax: 319 335 9565
Email: bento-soares@uiowa.edu
Tissue Procurement: Dr. Gregg Hageman
cDNA Library preparation: Dr. M. Bento Soares, Univeristy of Iowa
cDNA Library Arrayed by: Dr. M. Bento Soares, Univeristy of Iowa
DNA Sequencing by: Dr. M. Bento Soares, Univeristy of Iowa
Clone Distribution: Researchers may obtain clones from Research Genetics (www.resgen.com).
The following repetitive elements were found in this cDNA sequence: 1-21, >AT_rich#Low_complexity (matched compliment)
Seq primer: M13 Forward
POLYA=Yes.
FEATURES Location/Qualifiers
source 1. .300
/organism="Homo sapiens"
/mol_type="mRNA"
/db_xref="taxon:9606"
/clone="UI-E-CQ1-ada-e-09-0-UI"
/tissue_type="optic nerve"
/dev_stage="adult"
/lab_host="DH10B (Life Technologies) (T1 phage resistant)"
/clone_lib="UI-E-CQ1"
/note="Organ: eye; Vector: pT7T3-Pac (Pharmacia) with a modified polylinker; Site_1: EcoR I; Site_2: Not I; UI-E-CQ1 is a normalized cDNA library containing the following tissue(s): optic nerve. The library was constructed according to Bonaldo, Lennon and Soares, Genome Research, 6:791-806, 1996. First strand cDNA synthesis was primed with an oligo-dT primer containing a Not I site. Double stranded cDNA was ligated to an EcoR I adaptor, digested with Not I, and cloned directionally into pT7T3-Pac vector. The oligonucleotide used to prime the synthesis of first-strand cDNA contains a library tag sequence that is located between the Not I site and the (dT)18 tail. The sequence tag for this library is CCATTAAGTG. This library was created for the program, Gene Discovery in the Visual System, supported by National Eye Institute (NEI).
TAG_TISSUE=human optic nerve
TAG_LIB=UI-E-CQ1
TAG_SEQ=CCATTAAGTG"
ORIGIN

```
  Query Match            21.4%;  Score 212;  DB 12;  Length 300;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches  212;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        740 TTGGAGTGTGCAGATGCGATCTAGGTGTGTCCACCCGATGGGAGCTGCGGGCCGGGCAGA 799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        233 TTGGAGTGTGCAGATGCGATCTAGGTGTGTCCACCCGATGGGAGCTGCGGGCCGGGCAGA 174

Qy        800 TGCTGCCCCAGTACAAAGCTGATTTGGACCTGGGGCCTCTGGACTTCCCTGATTCTCTGC 859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        173 TGCTGCCCCAGTACAAAGCTGATTTGGACCTGGGGCGTCTGGACTTCCCTGATTCTCTGC 114

Qy        860 TTGCATCTCCAGCAAAGTCCTGTCCCGTTGGCTGCCTTCATCCACTCTCTCACTTCTCTG 919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        113 TTGCATCTCCAGCAAAGTCCTGTCCGGTTGGCTGCCTTCATCCACTCTCTCACTTCTCTG 54

Qy        920 CCTTCAGAGTAAAATTGCAAGATCTGTGGTGC 951
              ||||||||||||||||||||||||||||||||
Db         53 CCTTCAGAGTAAAATTGCAAGATCTGTGGTGC 22
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RESULT 13
BM687366
LOCUS BM687366 462 bp mRNA linear EST 28-FEB-2002
DEFINITION UI-E-CQ1-ada-e-09-0-UI.r1 UI-E-CQ1 Homo sapiens cDNA clone UI-E-CQ1-ada-e-09-0-UI 5', mRNA sequence.
ACCESSION BM687366
VERSION BM687366.1 GI:19000624
KEYWORDS EST.
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 462)
AUTHORS Bonaldo,M.F., Lennon,G. and Soares,M.B.
TITLE Normalization and subtraction: two approaches to facilitate gene discovery
JOURNAL Genome Res. 6 (9), 791-806 (1996)
MEDLINE 97044477
PUBMED 8889548
COMMENT Contact: Soares, MB
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Tel: 319 335 8250
Fax: 319 335 9565
Email: bento-soares@uiowa.edu
Tissue Procurement: Dr. Gregg Hageman
cDNA Library preparation: Dr. M. Bento Soares, Univeristy of Iowa
cDNA Library Arrayed by: Dr. M. Bento Soares, Univeristy of Iowa
DNA Sequencing by: Dr. M. Bento Soares, Univeristy of Iowa
Clone Distribution: Researchers may obtain clones from Research Genetics (www.resgen.com).
Seq primer: M13 Reverse.
FEATURES Location/Qualifiers
source 1. .462
/organism="Homo sapiens"
/mol_type="mRNA"
/db_xref="taxon:9606"
/clone="UI-E-CQ1-ada-e-09-0-UI"
/tissue_type="optic nerve"
/dev_stage="adult"
/lab_host="DH10B (Life Technologies) (T1 phage resistant)"
/clone_lib="UI-E-CQ1"
/note="Organ: eye; Vector: pT7T3-Pac (Pharmacia) with a modified polylinker; Site_1: EcoR I; Site_2: Not I; UI-E-CQ1 is a normalized cDNA library containing the following tissue(s): optic nerve. The library was constructed according to Bonaldo, Lennon and Soares, Genome Research, 6:791-806, 1996. First strand cDNA